November 12, 2003

James A. Deyo, D.V.M., Ph.D., DABT
Product Safety and Health Toxicology Team Leader
Eastman Chemical Company
100 North Eastman Road
Kingsport, TN 37662

Dear Dr. Deyo:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Dimethyl 1,4-cyclohexanedicarboxylate posted on the ChemRTK HPV Challenge Program Web site on July 14, 2003. I commend Eastman Chemical Company for their commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed Comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Eastman advise the Agency, within 60 days of this posting on the Web site, of any modifications to their submission. Please send any electronic revisions or comments to the following addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
Dimethyl 1, 4-Cyclohexanedicarboxylate

Summary of EPA Comments

The sponsor, Eastman Chemical Company, submitted a test plan and robust summaries to EPA for dimethyl 1,4-cyclohexanedicarboxylate (DMCD; CAS No. 94-60-0) dated June 17, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on July 14, 2003. The submission also includes data for the pure *trans* isomer (CAS No. 3399-22-2) and the structural analog 1,4-cyclohexanedicarboxylic acid (CHDA; CAS No. 1076-97-7).

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The submitter needs to provide measured vapor pressure and water solubility data following OECD guidelines.

2. Environmental Fate. The submitter needs to add 28-day values to the biodegradation summary.

3. Health Effects. Adequate data are available for all SIDS-level endpoints for the purposes of the HPV Challenge Program. The submitter needs to address a few deficiencies in the robust summaries.

4. Ecological Effects. The data provided for fish, aquatic invertebrate, and aquatic plants are adequate.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Dimethyl 1, 4-cyclohexanedicarboxylate Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data provided by the submitter for melting point, boiling point, and partition coefficient are adequate for the purposes of the HPV Challenge Program. According to OECD guidelines, if the estimated melting point is under 0 °C, then there is no need to provide measured data for this endpoint.

Vapor pressure. The submitter provided an estimated value of 0.0822 mm Hg (10.96 Pa). Estimated values over 10^{-5} Pa are not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured data for this endpoint following OECD guidelines.

Water solubility. The submitter provided an estimated value of 688.7 mg/L. An estimated value is not adequate for the purposes of the HPV Challenge Program. The submitter needs to provide measured data for this endpoint following OECD guidelines.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The data provided by the submitter for photodegradation, stability in water and fugacity are adequate for the purposes of the HPV Challenge Program.

Biodegradation. The submitter provided biodegradation data following OECD Guideline 301 B for a 35-day test. As the guideline test duration is 28 days, the submitter needs to include 28-day values in the summary.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for acute, reproductive and developmental toxicities on DMCD and for repeated-dose and genetic toxicities on the structural analog CHDA for the purposes of the HPV Challenge Program. In general, the justification for the use of the acid as an analog for the diester appears to be reasonable. However, the submitter needs to provide reference citations for the various points specified below.

(1) The test plan (p. 4) indicated that, in biological systems, the analog would be expected to be a demethylation product of the sponsored compound, based on similar findings for other short-to-medium length alkyl chain esters located at the one and four positions. The justification included several examples of cleavage of methyl units or ethylhexyl units from 1,4 diesters, but did not include any reference citations for these data.

(2) The test plan (p. 5) indicated acute oral LD_{50} values for the analog (1,903 mg/kg for males and 2,263 mg/kg for females, respectively), but no robust summary or reference citation was provided.

The submitter also needs to address a few deficiencies in the robust summaries.

Ecological Effects (fish, invertebrates, and algae)

The data provided for fish, daphnia, and green algae are adequate. However, the sponsor needs to provide missing water quality parameters.

Specific Comments on the Robust Summaries

Health Effects

The purity of the test material was missing for acute and genetic toxicity studies.

Acute toxicity. A robust summary for an acute oral toxicity study in rats exposed to DMCD was missing the gavage vehicle (if used) and the method for calculating the LD_{50}.

Reproductive and developmental toxicity. A robust summary for a GLP-compliant reproductive/developmental toxicity screening assay in rats exposed to DMCD in feed was missing the parental tissues that were evaluated for histopathology and the magnitudes of the reductions in feed consumption and body weight observed in parental males. The latter information is needed to determine whether the assignment of NOAEL values for parental males was justified.

Ecological Effects

Fish. The acute fish toxicity study summary was missing information on water chemistry measurements such as hardness and pH, as well as effects seen and number of fish affected at each concentration. These missing details need to be added to the summary.

Invertebrates. The acute invertebrate toxicity study summary was missing information on water chemistry measurements such as hardness and pH; on test group size; and on effects seen and number of daphnids affected at each concentration. These missing details need to be added to the summary.

Algae. In the algal toxicity study summary, pH was reportedly measured, but values were not reported in

the summary. These pH values should be reported in the summary.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.